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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,134	10/07/2005	Martin Hendrix	Le A 36 080	7514
35969	7590	04/20/2007		
JEFFREY M. GREENMAN BAYER PHARMACEUTICALS CORPORATION 400 MORGAN LANE WEST HAVEN, CT 06516			EXAMINER BALASUBRAMANIAN, VENKATARAMAN	
			ART UNIT	PAPER NUMBER
			1624	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/519,134

Applicant(s)

HENDRIX ET AL.

Examiner

Venkataraman Balasubramanian

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-4 and 6 is/are allowed.
- 6) ☒ Claim(s) 7 and 8 is/are rejected.
- 7) ☒ Claim(s) 9 and 10 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' response, which included cancellation of claims 11-13 and amendment to claims 1-4 and 6-8, filed on 1/2/6/2007, is made of record. Claims 1-4 and 6-10 are now pending. In view of applicants' response, the 112 first and second paragraph rejections of claims 1-4 and 6-13 pertaining to Markush choices and solvate, made in the previous office action have been obviated. However, the following 112 first paragraph rejection of method of use claims is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 8 are rejected under U.S.C. 112, first paragraph, because the specification while being enabling for treating breast cancer, Parkinson's disease and schizophrenia, does not reasonably provide enablement for treatment of any or all neurodegenerative diseases, any or all psychiatric disorders. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized above.

The instant method of use claims 7 and 8, are now drawn treating neurodegenerative diseases, and psychiatric disorders by inhibiting PDE 10A.

Instant claims, as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general

format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition of kinase by the instant compounds, instant claims reaches through treating any or all neurodegenerative diseases and all psychiatric disorders in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor of PDE 10A, based on limited assay, it is claimed that treating any or all neurodegenerative diseases, all psychiatric disorders in general, which there is no enabling disclosure. In addition, the scope of these claims includes treatment of various diseases, which is not adequately enabled solely based on the activity of the compounds provided in the specification at pages 27-31. The instant compounds are disclosed to have PDE 10A inhibitory activity and it is recited that the instant compounds are therefore useful in treating any or all diseases stated above for which applicants provide no competent evidence. It appears that the applicants are asserting that the embraced compounds because of their mode action as PDE 10A inhibitor that would be useful for all sorts of neurodegenerative diseases, psychiatric disorders and cancers. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host.

The scope of the claims involves all of the thousands of compounds of claim 1 as well as the thousand of diseases embraced by the terms neurodegenerative disease, and psychiatric disorder.

That a single class of compounds can be used to treat all diseases embraced in the claims is an incredible finding for which applicants have not provided supporting evidence. Moreover many if not most of diseases such as ALS or multiple sclerosis are very difficult to treat and despite the fact that there are many drugs, which can be used for "inflammatory condition".

The scope of the claims involves large number of compounds of claim 1 as well as numerous diseases embraced by the terms neurogenerative diseases and psychiatric disorders.

No compound has ever been found to treat all neurodegenerative disorders/diseases generally and provide prophylaxis of the said diseases. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to our present understanding of neurodegeneration process and psychiatric disorders. Thus, it is beyond the skill of neurologists today to get an agent to be effective against all neurodegenerative disorders/diseases generally. Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See *Ex parte Jovanovics*, 211 USPQ 907, 909; *In re Langer* 183 USPQ 288. Also note *Hoffman v. Klaus* 9 USPQ 2d 1657 and *Ex parte Powers* 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Lucas et al. *Pharmacological Reviews* 52 (3), 375-413, 2000.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

- 1) The nature of the invention: Therapeutic use of the compounds in treating disorders/diseases that require PDE inhibitory activity.
- 2) The state of the prior art: A recent publication expressed that the PDE inhibition effects are unpredictable and are still exploratory.
- 3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating any or all condition of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely

with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all condition and the state of the art is that the effects of PDE are unpredictable.

6) The breadth of the claims: The instant claims embrace any or all neurodegenerative diseases including those yet to be related to PDE.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re

Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

This rejection is same as made in the previous office action but now limited to claims 7 and 8. Applicants' traversal is not persuasive.

First of all, as noted above instant method of use claims are reach through claims. Based on the mode of action of instant compounds, it is claimed that treating any or all neurodegenerative diseases and all psychiatric disorders in general and thereby they lack adequate written description and enabling disclosure in the specification. Secondly, contrary to applicants' urging there is extensively undue experimentation to identify which of the genus of the compounds inhibit PDE and which would be useful for treating which neurogenerative disease or psychiatric disorder. Applicants' have not shown that treating a single disease or disorder is an objective enablement for treating any or all diseases or disorders. The issue is not making the said genus of compounds. It is the use of these compounds that is being addressed in the above rejection. In addition, because of one can obtain IC50 values, it does not mean that any or all diseases can be treated. There should be enabling disclosure showing that inhibition of the PDE resulted in treatment of any or all diseases generically claimed in the instant claims. Applicants have not provided any literature evidence for treating any or all neurogenerative disease or psychiatric disorder. As for applicants' quoting MPEP 2164.02, note MPEP requires objective enablement based on what is enabled and or enabling disclosure. Such is not the case with the instant claims.

Also see the PTO website <<<http://www.uspto.gov/web/offices/pac/dapp/1pecba.htm#7>>>ENABLEMENT DECISION TREE. Note MPEP 2164.08(b) which states that claims that read on "... significant numbers of inoperative embodiments would render claims nonenabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative.". Clearly that is the case here.

Hence, the rejection is proper and is maintained.

Allowable Subject Matter

Claims 1-4 and 6 are allowed, barring finding of any prior art in a subsequent search. Claims 9 and 10 are objected to as being dependent upon a rejected base claim, but would be allowable, barring finding of any prior art in a subsequent search, if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).


Venkataraman Balasubramanian

4/15/2007